Washington State Department of Health

ELABORATIONS

News and Issues for Washington's Clinical Laboratories

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Kidney Disease in Patients with Diabetes: An Opportunity for Prevention

by the Washington State Department of Health Diabetes Kidney Screening & Treatment Task Force (authors/affiliations listed at end of article)

Diabetes affects approximately 16 million people in the United States (US), but only 10 million are aware that they have the disease [1, 2]. Kidney disease affects 20-40% of persons with diabetes, and diabetic nephropathy is now the leading cause of endstage renal disease, or dialysis dependence, in the US. Intervention studies suggest that early treatment of hyperglycemia [3-6], hypertension [7-9] and microalbuminuria [7, 10-14] slow the progression of diabetic nephropathy. Treatment may also delay the need for dialysis and perhaps even prevent diabetic nephropathy occurrence in both Type 1 and Type 2 patients. Multiple studies in both Type 1 and Type 2 persons have shown that the use of angiotensin converting enzyme inhibitors (ACE-inhibitors) decreases progression of overt diabetic nephropathy and improve outcomes [3, 14].

- Primary care providers, including family physicians, have the most frequent contact with diabetic patients and, therefore, the greatest potential to affect their health.
- Over 200,000 people in Washington State have diabetes.
- Approximately 20-45% of people with diabetes will develop diabetic nephropathy, which is dependent upon the type and duration of diabetes.
- Each day one person with diabetes begins dialysis in Washington State.
- In a given year fewer than 40% of people with diabetes in Washington State receive screening for kidney function. (Department of Health Audit, 1999)

Due to the complex nature of diabetes, the preventable nature of most complications and the magnitude of associated healthcare costs, the Washington Department of Health developed a program of statewide diabetic public health surveillance and control activities for patients with diabetes. This collaborative evaluation of private and public health care systems found that evaluation of kidney function (tests of any kind) was being done in less than 40% of individuals with diabetes in the State, regardless of insurance type. In response to this audit, the Department of Health's Diabetes Control Program undertook a number of quality improvement projects, one of which included the formation of the Kidney Screening and Treatment Task Force. The task force, which included representatives from the medical and scientific laboratory communities in Washington, evaluated pre-existing protocols for the screening and treatment of microalbuminuria and diabetic nephropathy from the American Diabetes Association and National Kidney Foundation. These protocols were expanded to include more preventive measures based upon current evidence from the literature. Two algorithms, which summarize

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these recommendations (flow sheet and table formats), are included here on pages 5 and 6.

A Closer Look at the Algorithms:
Urinalysis for protein: A routine urinalysis should be performed in all Type 2 diabetic patients at the time of diagnosis and in Type 1 patients with a diagnosis of diabetes for 5 years or more. The urine dipstick detects a variety of proteins, although it is most sensitive to albumin.

- **Is the dipstick 1+ or greater for protein?** This patient has "**macro**albuminuria" and should be assessed with a quantitative measurement of total urine protein to quantitate the level of all the urine proteins present which includes albumin. If the level of total protein is greater than 1 gm/24 hr, referral to a nephrologist is recommended.
- **Is the dipstick less than 1+ for protein?** Patients already on an ACE-inhibitor should have a serum potassium and creatinine measured; if either is abnormal, the primary physician should consider consulting with a nephrologist. If both tests are normal, the patient should be continued on an ACE-inhibitor and have annual creatinine and potassium levels in addition to an annual urinalysis to measure protein progression. In addition, ***Renal Protective Recommendations*** (see box on page 3) for blood pressure control, glycemic control, lipid evaluation and lipid treatment should be considered.

Patients not on ACE-inhibitors should be retested for **micro**albuminuria annually.

Testing for microalbuminuria: There are several options for microalbuminuria testing, some of which include a random (spot) urine microalbumin to creatinine ratio (reported as mg microalbumin/mg creatinine or without units); a 24-hour urine collection that measures total mg of albumin in 24 hours (mg/24 hours); or a timed urine collection (reported as mcg albumin/min). Although the "gold standard" for screening has historically been the 24-hour collection, spot urine collections for albumin and creatinine can provide accurate information, and are often the easiest test to accomplish in the outpatient setting. First void or morning collections are preferred because of diurnal variation in albumin excretion. If the first voided specimen cannot be obtained, then urine should be collected at approximately the same time of the day for repeated collections in the same individual.

Because of the marked day-to-day variability in albumin excretion, and the potential for transient elevations in urine albumin excretion, it is recommended that two of three collections within a 3-6 month period show microalbuminuria.

- Confounding factors associated with an increase in microalbuminuria include poorly controlled diabetes, morbid obesity, acute illness with fever, pregnancy, high protein diet, urinary tract infection, congestive heart failure, acute water consumption >1L, hematuria, menstruation or a major stress such as surgery or anesthesia [15].
- Semiquantitative assays for albumin are available as test strips. These assays measure albumin concentration, so dilute urines or intra-individual variances in albumin excretion may yield a false-negative result. Semiquantitative assays are convenient and may be suitable for screening with the above caveats noted. These assays, however, are not sufficiently accurate for regular monitoring of patients.

Laboratory results can be presented in a variety of ways, depending on the sample collection used. Some laboratories may still report "normals" or a "reference range" for microalbuminuria that was based on an assessment of a "normal" population.

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Consultation or referral: An important part of the screening and treatment algorithms is the recommendation for consulting or referring to a nephrologist and to others who specialize in diabetic care, such as a diabetologist or endocrinologist. The evidence-based screening and treatment algorithm was developed with the input of primary care physicians, diabetologists and nephrologists, and reflects their collective recommendations for both consultation and referral. A patient whose quantitative urine protein test shows greater than one gram a day of protein or greater than one gram of protein per gram of creatinine requires referral to a specialist to determine the cause of the kidney disease (there may be causes other than diabetes), discuss treatment options, and educate the patient regarding the potential for dialysis. If the total protein does not exceed the above threshold but the potassium and/or creatinine are abnormal, consultation with a nephrologist is recommended.

What you as a laboratory practitioner can do to help protect the kidney function of your patients with diabetes:

- Help educate physicians and other providers about the ***Renal Protective Recommendations*** goals (see box in next column).
- Alert providers that a random (spot) urine is an acceptable specimen for microalbumin testing when urine creatinine is also included.
- Work with your medical colleagues to help them understand the results you are reporting to them. Laboratories may report results in a variety of ways e.g. “normal” or “clinical albuminuria.” Simplifying or standardizing reports may help interpretation and improve timely action. If your laboratory has the capacity to incorporate messages with the results e.g. “UA positive for protein, recommend quantitative total protein with 24-hour test or spot a.m. urine,” check with the ordering provider to see if this would be helpful. If microalbuminuria does not appear as a test on the laboratory slips you use, your lab may be able to help providers by changing the ordering form to make the process easier.

For more information on diabetes management, visit the Washington State Diabetes Collaborative website at www.doh.wa.gov/cfh/wsdc.

Renal Protective Recommendations:

- Strict blood pressure control of less than or equal to 130/80 mm/hg.
- Strict glucose control measured by a HbA1C less than or equal to 7.0% (*using an NGSP-certified method*).
- Lipid monitoring and control with a goal of a total cholesterol of less than 200 mg/dL, HDL greater than 45mg/dL, LDL of less than 100 mg/dL and triglycerides less than 150 mg/dL[16].

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References:

1. Harris, M.I., et al., *Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in U.S. population aged 20-74 yrs.* Diabetes, 1987. **36**(4): p. 523-34.
2. Anonymous, *Facts and Figures*. 2000, American Diabetes Association.
3. Anonymous, *The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group.* New England Journal of Medicine, 1993. **329**(14): p. 977-86.
4. Ohkubo, Y., Kishikawa, H., Araki, E., Miyata,T., Isami, S., Motoyoshi, S., Kojima, Y., Furuyoshi, N., Shichiri, M., *Intensive insulin therapy prevents the progression of diabetic microavascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6 year study.* Diabetes Research and Clinical Practice, 1995. **28**: p. 103-117.
5. Anonymous, *Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with Type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group [published erratum appears in Lancet 1999 Aug 14;354(9178):602] [see comments].* Lancet, 1998. **352**(9131): p. 837-53.
6. Anonymous, *Effect of intensive blood-glucose control with metformin on complications in overweight patients with Type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group [see comments] [published erratum appears in Lancet 1998 Nov 7;352(9139):1557].* Lancet, 1998. **352**(9131): p. 854-65.
7. Lewis, E.J., et al., *The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. The Collaborative Study Group [see comments] [published erratum appears in N Engl J Med 1993 Jan 13;330(2):152].* New England Journal of Medicine, 1993. **329**(20): p. 1456-62.
8. Anonymous, *Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group [see comments] [published erratum appears in BMJ 1999 Jan 2;318(7175):29].* BMJ, 1998. **317**(7160): p. 703-13.
9. Anonymous, *Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in Type 2 diabetes: UKPDS 39. UK Prospective Diabetes Study Group [see comments].* BMJ, 1998. **317**(7160): p. 713-20.
10. Mathiesen, E.R., et al., *Efficacy of captopril in postponing nephropathy in normotensive insulin dependent diabetic patients with microalbuminuria [see comments].* BMJ, 1991. **303**(6794): p. 81-7.
11. Anonymous, *Randomised placebo-controlled trial of lisinopril in normotensive patients with insulin-dependent diabetes and normoalbuminuria or microalbuminuria. The EUCLID Study Group [see comments].* Lancet, 1997. **349**(9068): p. 1787-92.
12. Ravid, M., et al., *Long-term renoprotective effect of angiotensin-converting enzyme inhibition in non-insulin-dependent diabetes mellitus. A 7-year follow-up study [see comments].* Archives of Internal Medicine, 1996. **156**(3): p. 286-9.
13. Ravid, M., et al., *Use of enalapril to attenuate decline in renal function in normotensive, normoalbuminuric patients with Type 2 diabetes mellitus. A randomized, controlled trial.* Annals of Internal Medicine, 1998. **128**(12 Pt 1): p. 982-8.
14. Anonymous, *Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators [see comments].* Lancet, 2000. **355**(9200): p. 253-9.
15. Mogensen, C.E., et al., *Microalbuminuria and potential confounders. A review and some observations on variability of urinary albumin excretion.* Diabetes Care, 1995. **18**(4): p. 572-81.
16. *Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III).* Jama, 2001. **285**(19): p. 2486-97.

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Diabetes Renal Disease Prevention, Detection, Treatment and Monitoring

Type 1 and Type 2; age 12 years and older with no overt renal disease

November 2001

Washington State Clinical Advisory Council to the Washington State Department of Health
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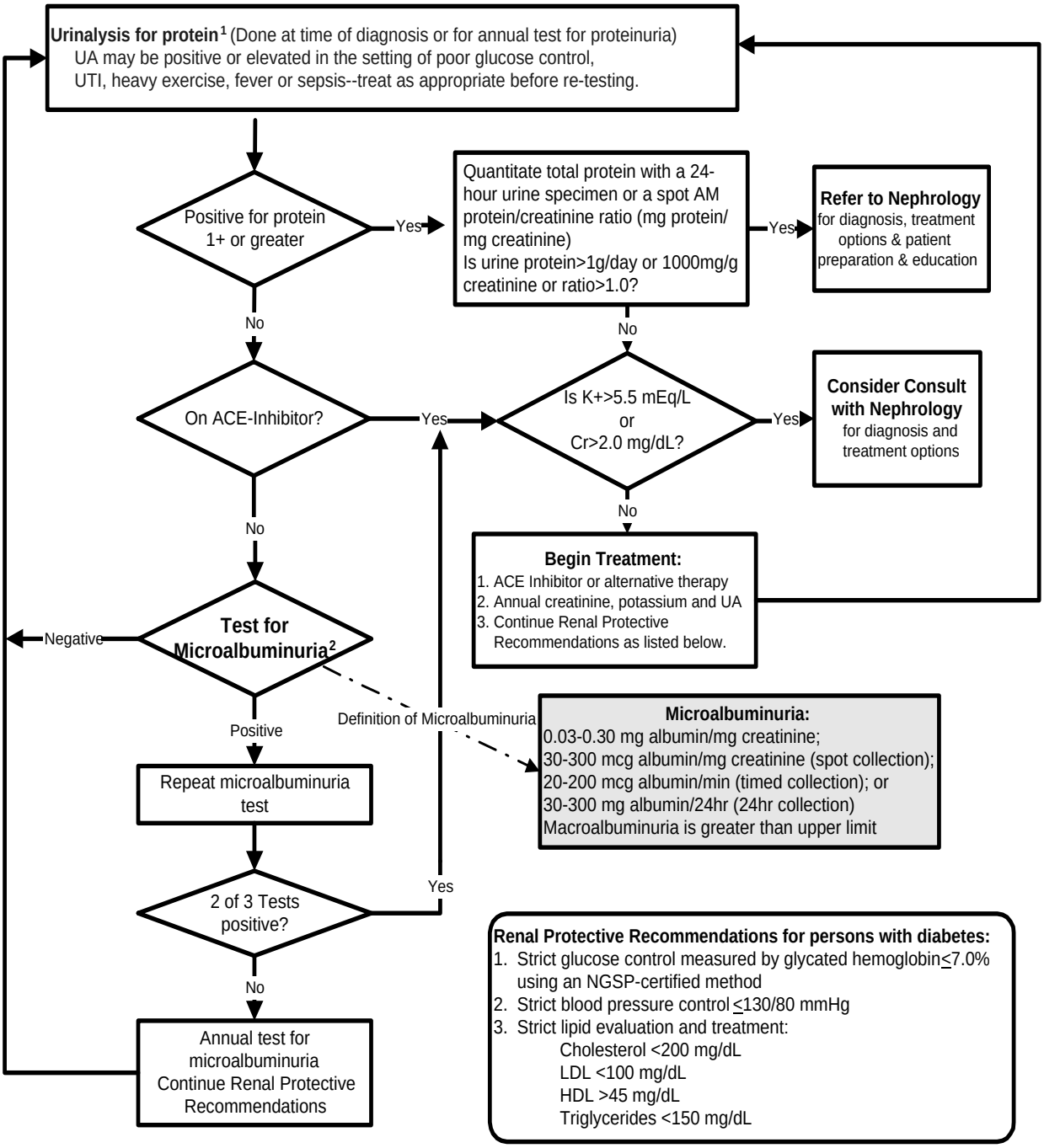
www.doh.wa.gov/cfh/wsdc



Renal Protective Recommendations for persons with diabetes:

1. Strict glucose control measured by glycated hemoglobin ≤7.0% using an NGSP-certified method
2. Strict blood pressure control ≤130/80 mmHg
3. Strict lipid evaluation and treatment:
   - Cholesterol <200 mg/dL
   - LDL <100 mg/dL
   - HDL >45 mg/dL
   - Triglycerides <150 mg/dL

[1]Check with your lab on test choice and availability, specimen collection, preference, and interpretation.

[2]Most labs use a very sensitive method to measure albumin in the microalbumin range. Check with your lab on test choice and availability, specimen collection, preference, and interpretation.

FOR EDUCATIONAL PURPOSES ONLY

The individual clinician is in the best position to determine which tests are most appropriate for a particular patient

Renal Disease In Diabetes

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FOR EDUCATIONAL PURPOSES ONLY

The individual clinician is in the best position to determine which tests are most appropriate for a particular patient.

Screening and Monitoring	Treatment and Monitoring	Risk of ESRD
Urinalysis for protein* **Less than 1+ protein:** Test for **microalbuminuria**** with either: 1. Spot AM urine for mg microalbumin/mg creatinine (ratio)***;** or 2. Timed urine collection for mcg albumin/min; or 3. 24 hour urine collection for total mg albumin/24 hours. **NOTE:** See the following two boxes for interpretation of results for these tests.	**Protective Recommendations for all patients** 1. Strict glucose control (HbA1C less than or equal to 7.0% using an NGSP-certified method); 2. Strict blood pressure control (less than or equal to 130/80); 3. Strict lipid control (cholesterol less than 200 mg/dL, LDL less than 100 mg/dL, HDL greater than 45 mg/dL, triglycerides less than 150 mg/dL).	
1. Spot AM urine microalbumin/creatinine ratio less than 0.030 on 2 of 3 tests (to rule out false positives*); or 2. Urine albumin less than 20 mcg/min on timed urine collection; or 3. Total urine albumin less than 30 mg on 24-hour urine collection.	**No microalbuminuria** 1. Repeat test for microalbuminuria** **annually;** 2. Continue **Protective Recommendations** as above; 3. If patient already on ACE inhibitor, check serum creatinine and K+ (see #4 below).	**Low**
1. Spot AM urine microalbumin/creatinine ratio 0.030 to 0.300 on 2 of 3 tests (to rule out false positives*); or 2. Urine albumin 20 to 200 mcg/min on timed urine collection; or 3. Total urine albumin 30 to 300 mg on 24 hour urine collection.	**Microalbuminuria (incipient nephropathy)** 1. If serum creatinine less than 2 mg/dL and K+ less than 5.5 mEq/L, treat with ACE inhibitor; 2. Continue **Protective Recommendations** as above; 3. Check serum creatinine and K+ and UA for gross proteinuria annually; 4. If creatinine greater than 2 mg/dL or K+ greater than 5.5 mEq/L; **consider consult with nephrologist.**	**Mod: incipient nephro-pathy**
Greater than or equal to 1+ protein, or **Spot AM urine albumin/creatinine ratio greater than 0.300 on 2 of 3 tests (to rule out false positives*).** Check total gm urine protein on 24-hour urine collection, or spot AM urine protein/creatinine ratio. 1. Total urine protein greater than 500 mg but less than 1 gram on 24-hour urine collection; or 2. Spot AM urine protein/creatinine ratio greater 0.5 but less than 1.0.	**Macroalbuminuria/gross proteinuria (overt nephropathy)** 1. Continue treatment as for microabuminuria above; 2. Consider consult with nephrologist.	**High: overt nephro-pathy**
1. Total urine protein greater than 1 gram in 24 hours; or 2. Spot AM urine protein/creatinine ratio greater than 1.0.	**Marked proteinuria (severe renal disease)** Refer to nephrologist for education and preparation for dialysis	**Extremely high: pending ESRD**

* UA protein or spot AM urine microalbumin/creatinine ratio may be positive or elevated in the setting of poor glucose control, UTI, heavy exercise, fever or sepsis – treat as appropriate before re-testing

******Most labs use a very sensitive method to measure albumin in the microalbumin range. Check with your lab on test choice and availability, specimen collection, preference, and interpretation.

Laboratory-Related Internet Sites

In April 2001, a questionnaire was sent to a network of laboratories in the Pacific Northwest to learn how laboratorians use the Internet for work-related purposes. We shared the findings of that study in the September 2001 issue of Elaborations and provided a list of some of the websites that the respondents said they used. In this issue, we are sharing more website addresses (uniform resource locators [URLs]) for your interest. A complete listing of websites gathered from this study can be found on the Centers for Disease Control and Prevention (CDC) website at: www.phppo.cdc.gov/dls/mlp/pnlmsmn.asp

NOTE: The following summarizes the data collected from network participants. We do not intend to endorse or promote any agency, organization, corporation or website listed. Website addresses were accessed in June 2001 by the author to confirm their accuracy. Changes in website addresses and links may have occurred since then.

REFERENCE LABORATORIES PROVIDING TESTING SERVICES

Antibody Assay Laboratories		www.antibodyassay.com
ARUP Laboratories		www.arup-lab.com
Berkeley Heart Lab		www.berkeleyheartlab.com
Diagnology		www.diagnology.com
Duke University Lab		www.duke.edu
Genetests		www.genetests.org
LabCorp		www.labcorp.com
Labs NW		www.labsnw.com
Med Tox		www.medtox.com
National Medical Services		www.nmslab.com
OHSU		www.ohsu.edu
PAML		www.paml.com
Puget Sound Blood Center		www.psbc.org
Quest Diagnostics		www.questdiagnostics.com
Specialty Laboratories	www.specialty.com	www.datapassportmd.com

PROFESSIONAL ORGANIZATIONS

AAB-American Association of Bioanalysts		www.aab.org
AABB-American Association of Blood Banks		www.aabb.org
AACC-American Association of Clinical Chemists		www.aacc.org
AAFP-American Academy of Family Physicians		www.aafp.org
AAP-American Academy of Pediatrics		www.aap.org
ABPA-American Backflow Prevention Association		www.abpa.org
ACHA-American College Health Association		www.acha.org
ADA-American Diabetes Association		www.diabetes.org
Advance		www.advanceformlp.com
AMA-American Medical Association		www.ama-assn.org
AMT-American Medical Technologists		www.amt1.com
ANA-American Nurses Association - safety information for nurses		www.needlestick.org
APHA-American Public Health Association		www.apha.org
APHL-American Public Health Laboratories		www.aphl.org
ASC-American Society of Cytopathology		www.cytopathology.org
ASCLS-American Society for Clinical Laboratory Science		www.ascls.org
ASCP-American Society of Clinical Pathologists		www.ascp.org
ASM-American Society for Microbiology		www.asm.org
CAP-College of American Pathologists		www.cap.org
CLMA-Clinical Laboratory Management Association		nwww.clma.org
Medscape Med Pulse	via e-mail:	news@medpulse.medscape.com
MGMA-Medical Group Management Association		www.mgma.org
NACB-National Academy of Clinical Biochemistry		www.nacb.org
NAACLS-National Accrediting Agency for Clinical Lab Sciences		www.naacls.org
NCA-National Credentialing Agency		www.nca-info.org
Nursing Insider	via e-mail:	anamember@lists.ana.com
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Calendar of Events

WSSCLS/NWSSAMT Spring Meeting
April 25-27, 2002 Everett

Northwest Medical Laboratory Symposium
October 2002 Portland

9th Annual Clinical Laboratory Conference
November 2002 Seattle

Contact information for the events listed above can be found on page 2. The Calendar of Events is a list of upcoming conferences, deadlines, and other dates of interest to the clinical laboratory community. If you have events that you would like to have included, please mail them to ELABORATIONS at the address on page 2. Information must be received at least one month before the scheduled event. The editor reserves the right to make final decisions on inclusion.

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